ABSTRACT

Crystal growth can be initiated and controlled by dynamically controlled vapor diffusion or temperature change. In one aspect, the present invention uses a precisely controlled vapor diffusion approach to monitor and control protein crystal growth. The system utilizes a humidity sensor and various interfaces under computer control to effect virtually any evaporation rate from a number of different growth solutions simultaneously by means of an evaporative gas flow. A static laser light scattering sensor can be used to detect aggregation events and trigger a change in the evaporation rate for a growth solution. A control/follower configuration can be used to actively monitor one chamber and accurately control replicate chambers relative to the control chamber. In a second aspect, the invention exploits the varying solubility of proteins versus temperature to control the growth of protein crystals. This system contains miniature thermoelectric devices under microcomputer control that change temperature as needed to grow crystals of a given protein. Complex temperature ramps are possible using this approach. A static laser light scattering probe also can be used in this system as a non-invasive probe for detection of aggregation events. The automated dynamic control system provides systematic and predictable responses with regard to crystal size. These systems can be used for microgravity crystallization projects, for example in a space shuttle, and for crystallization work under terrestial conditions. The present invention is particularly useful for macromolecular crystallization, e.g. for proteins, polypeptides, nucleic acids, viruses and virus particles.